TRANSCRIPTIONAL PROFILE OF HUMAN PLACENTA EXPLANTS IN RESPONSE TO INTERACTION WITH *Plasmodium falciparum*

PERFIL TRANSCRIPCIONAL DE LOS EXPLANTES DE PLACENTA HUMANA EN RESPUESTA A LA INTERACCIÓN CON *Plasmodium falciparum*

Ana María Garcia[1]; Carolina López–Guzman[2]; Ana María Vasquez[3] & Cesar Hernando–Segura[3]

[1]Researcher, Malaria Group, University of Antioquia. Medellín – Colombia.
[2]PhD student, Malaria Group, University of Antioquia. Medellín – Colombia.
[3]Research professor, Malaria Group, University of Antioquia. Medellín – Colombia.

ana.garcia6@udea.edu.co

Malaria is an infectious disease caused by intracellular parasites of the genus *Plasmodium*, which is transmitted to humans by the bite of infected female mosquitoes of the genus *Anopheles*. This infection in pregnant women is a major cause of maternal illness and a threat to neonatal health. During Plasmodium falciparum infection, parasites attach to the placenta as a result of the interaction between the parasitic antigen VAR2CSA and the chondroitin sulfate A (CSA) receptor expressed on syncytiotrophoblast (ST) cells. The TS is the epithelial layer that lines the placental villi and performs essential functions for fetal development. The maternal inflammatory response is known to contribute to maternal and fetal complications during *P. falciparum* infection, however, little is known about other processes that are activated or dysregulated in ST and placental tissue. An approach to know the mechanisms of damage or pathogenesis is to study the profiles of gene expression or transcriptomics, sequencing the total RNA expressed during infection, which represents a powerful tool to analyze the response of cells and tissues and identify new genes and pathways involved in pathogenesis. This work aimed toto entify changes in gene expression in human placental explants from healthy donors in an ex vivo model of infection with *Plasmodium falciparum*. Human placenta explants were used as a study model, as they represent the behavior of TS in a context that maintains the cellular architecture of the tissue *in vivo*. The placental explants were obtained from healthy donors, with term delivery and cultured for 48h. Subsequently, erythrocytes infected with *P. falciparum* were added. to a parasitemia of 10% and uninfected erythrocytes as controls. After 24 hours of infection, tissues were collected for RNA isolation and histological studies and supernatants for feasibility studies. Gene expression profiles of explants exposed to erythrocytes infected with *P. falciparum* were characterized by RNA sequencing (RNA-Seq). We found 165 protein-coding genes that showed a significant change in their expression among explants exposed to infected erythrocytes compared to controls (exposed to uninfected red blood cells). Exposure to infected red blood cells induced overexpression of genes associated with inflammatory response, lymphocyte activation, and cell adhesion. The gene with the

greatest change in its expression with respect to the controls was PAEP. Other gene genes such as IRF4, THEMIS, ZNG683, KISS1R and MMP-17 were also upregulated in explants exposed to *P. falciparum*. Together, these data suggest that in response to infection there is positive regulation of genes that could be involved in adverse effects, since several of the genes expressed encode, proteins associated with pathologies such as preeclampsia and preterm birth. The need to continue with additional studies to confirm the role of these genes and their products in the context of *Plasmodium falciparum* infection during pregnancy is highlighted.

Keywords: RNAseq – *Plasmodium falciparum* – Chorionic Villi – placenta – malaria